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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/007,489	12/05/2001	Elizabeth Gay Frayne		2256

7590 12/05/2003  
Elizabeth Frayne  
2027 Galvin Ln. #1  
Diamond Bar, CA 91765

EXAMINER
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KHARE, DEVESH

ART UNIT	PAPER NUMBER
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1623

DATE MAILED: 12/05/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/007,489

**Applicant(s)**

FRAYNE, ELIZABETH GAY

**Examiner**

Devesh Khare

**Art Unit**

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) g.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

Applicant's election the claims 1-5 of Group I (Paper # 10), is acknowledged. The 'Amendment A' received on 10/02/2003 has been entered. Claims 6-13 have been cancelled. The title has been accepted. The substituted specification and drawings have been entered.

Claims 1-5 are currently pending in this application.

**35 U.S.C. 112, second paragraph rejection**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under the second paragraph of 35 U.S.C. 112, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) The term "generating phosphorothioate oligo mixtures" in claim 1 is a relative term, which render the claims indefinite. The term "generating phosphorothioate oligo mixtures" does not define whether the generation is meant in "*in vitro*" or "*in vivo*", the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

(B) Regarding claim 1 (3), the phrase "such that" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). The phrase also renders claims depending from claim 1 indefinite.

(C) Claim 4 recites the limitation "method of claim 1 wherein the cells cultured". There is insufficient antecedent basis for this limitation in the claim because claim 1 does not recite the cells.

(D) Claim 5 recites the limitation "method of claim 1 using other derivatives of phosphate". There is insufficient antecedent basis for this limitation in the claim because claim 1 does not recite derivatives of phosphate.

(E) Regarding claim 5, the phrase "such as" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

### **Information Disclosure Statement**

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

### **35 U.S.C. 103(a) rejection**

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.*

Claims 1,3- 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sayers et al. (Sayers) (Directed Mutagen. 49-69, 1991).

Claims 1,3-5 are drawn to a method of generating phosphorothioate oligo mixtures comprising:

1. growing a single-stranded recombinant DNA in a media containing thio-phosphate.
2. harvesting the single-stranded phage and purifying the DNA
3. fragmentation of the insert DNA to yield oligo mixtures.

Additional claim limitations include media consisting of a mixture of thiophosphate and inorganic phosphate; cells used are of prokaryotic or eukaryotic origin; and derivatives of phosphate.

Sayers teaches the phosphorothioate-based oligonucleotide directed mutagenesis method for repairing the DNA *in vitro* (see page 49, Intro. 3<sup>rd</sup>. para.). Sayers discloses that a phosphorothioate group may be incorporated exclusively into the strand of a newly synthesized RF-IV DNA in a cell (page 50, first para. and Figure 1). Sayer also discloses the phosphorylation of the mismatch primer wherein the phosphorylation is catalysed by the enzyme polynucleotide kinase and requires ATP and the said phosphorylated primer is then combined with the template DNA (see page 55, 2<sup>nd</sup> para. Preparation of RF-IV DNA). While the Sayers's method of generating phosphorothioate oligo mixtures is closely analogous to the applicant's method,

Sayers's method of generating phosphorothioate oligo mixtures differ from applicant's method that it is directed to the phosphorylation of the mismatch primer in a cell.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to modify the method of generating phosphorothioate oligo mixtures in a cell as taught by Sayers, because Sayers had disclosed that oligonucleotide-directed mutagenesis allows the molecular biologist to alter a defined nucleotide sequence within a gene in a precise manner to use in the applications such as protein engineering and in the study of molecular recognition (see page 49, Introduction, first para.).

A review of the prior art revealed no references that could be appropriately applied on claim 2, claiming a method for *in vivo* incorporation of thiophosphate into nucleotide precursor pools of ds DNA, ss DNA, and/or RNA.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Devesh Khare whose telephone number is (703)605-

1199. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be

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reached at 703-308-4624. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Devesh Khare, Ph.D.,JD(3Y).  
Art Unit 1623  
November 28, 2003



JAMES O. WILSON  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600